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| 10/565,494 | 01/20/2006 | Yaeta Endo | 319005001 | 2077 |

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KILYK & BOWERSOX, P.L.L.C.
400 HOLIDAY COURT
SUITE 102
WARRENTON, VA 20186

| EXAMINER | |
|---|---|
| FOSTER, CHRISTINE E | |
| **ART UNIT** | **PAPER NUMBER** |
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/565,494 | ENDO ET AL. | |
| | Examiner | Art Unit | |
| | Christine Foster | 1641 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *01 October 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-15* is/are pending in the application.

4a) Of the above claim(s) *7 and 12-15* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6 and 8-11* is/are rejected.

7)☒ Claim(s) *3-5* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *20 January 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

1. Applicant's amendment, filed 10/1/08, is acknowledged and has been entered. Claims 1-6 and 8-11 were amended. Accordingly, claims 1-15 are pending in the application, with claims 7 and 12-15 currently withdrawn. Claims 1-6 and 8-11 are subject to examination below.

### *Priority*

2. Acknowledgment is made of the present application as a proper National Stage (371) entry of PCT Application No. PCT/JP04/11567, filed 8/2/2004, which claims priority under 35 U.S.C. 119(e) from provisional application No. 60/542,201, filed on 2/5/2004. Acknowledgment is also made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d) to Application No. 2003-288859, filed on 8/7/2003 in Japan.

3. Applicant's filing on 10/1/2008 of a certified English translation of provisional application No. 60/542,201 in accordance with 37 CFR 1.78(a)(5) is acknowledged.

### *Objections/ Rejections Withdrawn*

5. The objections to claims 1-6 and 8-11 as set forth in the previous Office action have been withdrawn in response to Applicant's amendments.

6. The rejections under § 112, 2nd paragraph as set forth in the previous Office action have been withdrawn in response to Applicant's amendments.

7. The rejections of claim 1-2, 6, and 8 under § 102 as being anticipated by Kuroita et al. have been withdrawn in response to Applicant's amendments to recite that the protein chip reagent includes a specific translation template.

### *Claim Objections*

8. Claims 3-5 are objected to because of the following informalities:

9. Claim 3 is objected to because due to the grammatical structure of the claim, it is unclear what subject the clause "for adding to different wells of a container…" is intended to modify. For example, is the "translation reaction solution" for adding to different wells? Or the deliquescent substance?

10. Claim 4 recites that "an amount of the deliquescent substance in the freeze-dried preparation is less than 0.01 part **by weight by weight**" (emphasis added). It appears that the phrase "by weight" has been inadvertently duplicated in the claim.

11. Claim 4 has extra spaces preceding the comma in line 20 in the phrase "a protein synthesized from the translation template , the protein being modified for fixation...".

12. Claim 5 recites that "the modification for fixation is at least one which is selected from…". The language --the modification for fixation is selected from the group consisting of-- is suggested for clarity.

### *Claim Rejections - 35 USC § 112*

13. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

14. Claims 4-5 and 10-11 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the

relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

15. Claim 4, as instantly amended, now recites "a protein synthesized from the translation template ,[sic] the protein being modified for fixation...". The claim can now be interpreted as meaning that the protein chip reagent includes synthesized protein as one of the elements (see rejection under § 112, 2nd paragraph below). In other words, the claim could be read as meaning that a protein synthesized from the translation template is provided as part of the freeze-dried protein chip reagent.

Applicant's reply states that the amendments are typographical or grammatical in nature and supported throughout the present application and claims as originally filed (Reply, page 8). However, no support could be found in the application as originally filed for a freeze-dried protein chip reagent that includes both a translation template as well as a protein that is synthesized from the translation template.

As originally filed, claim 4 recited "protein synthesized from the translation template is modified for fixation". However, this at best conveyed that the resulting protein synthesized using the protein chip reagent would be modified, invoking limitations as to the nature of the translation template. The claim indicates that the translation templates are "for making two or more kinds of proteins" (see lines 16-18), suggesting that the intended downstream use of the reagent is for protein synthesis. Similarly, the specification makes clear that the purpose of the protein chip reagent is for cell-free protein synthesis. In other words, the protein chip reagent is designed to produce protein after it is dissolved and reconstituted from its freeze-dried state. See especially pages 27-28 of the specification. By contrast, the claim now implies that the protein

itself is provided, together with the translation template and other ingredients, in freeze dried form. One skilled in the art would not envisage possession of protein chip reagents as claimed, in which the product of the cell-free protein synthesis reaction would be included in the freeze-dried reagent itself.

16. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

17. Claims 1-6 and 8-11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

18. Claim 1, as instantly amended, recites:

> 1. (Currently amended): A protein chip reagent utilizing a cell-free protein synthesis system which comprises the following elements:
>
> ~~a.~~ a translation reaction solution containing cell extract for a cell-free protein synthesis comprising a wheat embryo extract wherefrom endosperm components and low-molecular weight protein synthesis inhibitors are substantially removed, substances necessary for protein synthesis containing a substrate and an energy source, and a specific translation template ~~is added~~ for adding to ~~each~~ one or more different ~~well~~ wells of a container which is partitioned in plural sections;

Due to the grammatical structure of the claim, it is unclear whether Applicant intends that the "translation reaction solution" to include only the cell extract (comprising wheat embryo extract); or alternatively to include cell extract, substances necessary for protein synthesis, and

the specific translation template. In other words, it is not clear whether all of the listed ingredients are provided together as part of the translation reaction solution, or simply as part of the protein chip reagent.

19. Similarly, in claims 2-4 it is not clear whether the ingredients listed in lines 3-7 of the claims are all components of the translation reaction solution or not.

20. Claims 3-4 recite "a specific translation template" in line 6 of the claims, which is one of the ingredients of the protein chip reagent (and possibly also part of the translation reaction solution; see above). Lines 7-8 of the claims invoke "for adding to different wells of a container…" The claims also later refer to "a plurality of different translation templates are contained in each of the different wells of the container". The claims are confusing because it is unclear whether the container is actually part of the claimed protein chip reagent or not. The terminology "for adding to different wells of a container" invokes a possible intended use of the claimed ingredient(s) earlier recited but does not clearly require that the container be part of the reagent. However, "a plurality of different translation templates are contained in each of the different wells of the container" implies that the protein chip reagent includes multiple different templates that are provided in a container. Clarification is needed as to whether the protein chip reagent includes the partitioned container or not.

In addition, what is the relationship of the "specific translation template" to the "plurality of different translation templates"? Is the former one of the latter?

21. Claim 4 recites that "the protein chip reagent is a freeze-dried preparation prepared by freeze drying an amount of the deliquescent substance in the freeze-dried preparation is less than 0.01 part by weight...". The claim implies that the freeze-dried preparation is prepared by freeze-

drying the freeze-dried preparation itself. Applicant's intended meaning is unclear. It would seem that the freeze-dried preparation would not be freeze-dried until after freeze-drying. In addition, the claim is a run-on sentence, which further obscures the meaning.

22. Claim 4 also recites "a protein synthesized from the translation template ,[sic] the protein being modified for fixation...". The scope of the claim is unclear because it is not clear whether Applicant intends that the protein is a component part of the freeze-dried protein chip reagent, or alternatively whether the freeze-dried protein chip reagent is capable of synthesizing protein that is modified for fixation.

As originally filed, claim 4 recited "protein synthesized from the translation template is modified for fixation". However, this at best conveyed that the resulting protein synthesized using the protein chip reagent would be modified, invoking limitations as to the nature of the translation template. The claim indicates that the translation templates are "for making two or more kinds of proteins" (see lines 16-18), suggesting that the intended downstream use of the reagent is for protein synthesis. By contrast, the claim could now be interpreted as meaning that the product of the protein synthesis reaction, the protein itself, is provided together with the translation template and other ingredients, in freeze dried form.

### *Claim Rejections - 35 USC § 103*

23. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

24. Claims 1-6 and 8-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kuroita et al. US 2003/0199076 A1 in view of He et al. (WO 02/14860) and Zuk et al. (4,208,479).

Kuroita et al. teach a reagent composition for cell-free protein synthesis that is provided in a freeze-dried state for stability (the abstract, [0001], [0004], [0006], [0102]). The reagent composition contains a cell extract, which may be from wheat embryo without endosperm and almost free of protein synthesis inhibitors such as ribosome specific glycosidase (i.e., translation reaction solution). See [0003], [0035], [0055], [0111]. The composition preferably also contains an energy source, template mRNA, substrate amino acids, etc., (i.e., substances necessary for protein synthesis) which may be provided in kit form. See [0002], [0027], [0062], [0064], [0089]-[0098].

Regarding the recitation that the specific translation template is "for adding" to one or more wells of a partitioned container, such statements are interpreted as being directed to the intended use of the claimed reagent and do not clearly require the use of a partitioned container. The Examiner notes that no structural difference is apparent as a result of this statement of the intended use of the claimed reagent. Therefore, since the components of the freeze-dried reagent of Kuroita et al. would also be capable of being added to wells of a partitioned container, it meets the claim.

With respect to the "deliquescent substance" recited in claims 2-4, Kuroita et al. further teach that the reagent composition includes an amount of a deliquescent material that is no more than 0.01 part by weight per part of protein [0011], [0024], [0034], [0102]. As discussed above, the recitation of components "for adding" to one or more wells apparently refers to the intended

use of the components. In the instant case, the deliquescent substance would be capable of performing the intended use of being added to wells and therefore reads on the claim.

With respect to the "protein" recited in claims 2-4, the composition preferably comprises a bioactive protein for cell-free protein biosynthesis [0015].

The teachings of Kuroita et al. differ from the instantly claimed invention in that the reference fails to specifically teach that the protein chip reagent includes a "specific translation template". In addition, with respect to the "plurality of different translation templates" recited in claims 3-4, Kuroita et al. discuss how a template is needed for the protein synthesis reaction [0062] but fail to specifically teach that the template is included in the freeze-dried reagent. In addition, with respect to claims 4-5, Kuroita et al. fail to specifically teach protein being "modified for fixation".

He et al. teach cell-free protein synthesis systems that employ an array format, allowing the advantage of handling and investigation of multiple samples (pages 1 and 7-8). This allows for protein arrays to be prepared, so that the functions of thousands of proteins can be examined in parallel (ibid). In one embodiment, the in vitro synthesis reactions can be performed in wells of multiwell plates, using individual nucleic acids such as mRNA as starting material (i.e., specific translation templates). See page 7.

Zuk et al. teach that in performing assays it is a matter of substantial convenience, as well as providing significant enhancement in accuracy to provide the reagents combined in a kit form and preferably in a single vessel (column 22, lines 21-44). Furthermore, it is desirable to combine as many reagents as possible in a single vessel for each step of the assay.

Therefore, when taken together with the teachings of Kuroita et al. and He et al. which establish that a template is required for protein synthesis assays in addition to wheat germ extract, etc., it would have been obvious to one of ordinary skill in the art to combine these necessary ingredients together for convenience and accuracy as taught by Zuk et al..

With respect to claims 3-4, which invoke a "plurality of different translation templates", when taken together with the teachings of He et al. that thousands of proteins can be examined in parallel using individual nucleic acids such as mRNA as starting material (i.e., a plurality of different translation templates), it would have been further obvious to one of ordinary skill in the art to include individual templates for protein synthesis as taught by He et al. in the protein chip reagent of Kuroita et al. so that an array of many different proteins could be synthesized by cell free protein synthesis and then examined in parallel. The advantage of handling and parallel investigation of multiple proteins produced by cell-free protein translation provides motivation to combine the teachings of He et al. with those of Kuroita et al., which also relates to cell-free protein translation.

It is not entirely clear whether multi-well container is actually a component of the claimed protein chip reagent or not (see rejections under § 112, 2nd paragraph above). However, in light of the teachings of He et al. that in vitro synthesis reactions can be performed in wells of multiwell plates so as to create an array format, it would have been further obvious to provide the different templates (as part of the protein chip reagent) in wells of multiwell plates so as to allow for handling and investigation of multiple samples.

With respect to claims 4-5, it is not entirely clear whether the "protein synthesized from the translation template [that is] modified for fixation" is intended to be part of the claimed

reagent, or alternatively whether Applicant intends that the claimed protein chip reagent is capable of producing such proteins (see rejections under § 112, 2nd paragraph above). When the latter interpretation is adopted, the reference teachings read on the claims for the following reasons.

He et al. further teach adapting proteins to be synthesized by in vitro translation for rapid isolation, immobilization or identification by inclusion of modifications for fixation (sequences such as hexahistidine or other peptide tags). See in particular the abstract and pages 7 and 12. This allows for the proteins to be captured onto wells or other surfaces that have immobilizing reagents (i.e., substance having affinity to a substance added by the modification).

Therefore, it would have been further obvious to incorporate a hexahistidine or other peptide tag as taught by He et al. in the nascent proteins to be synthesized by the protein chip reagent of Kuroita et al. so that the translated proteins could be rapidly isolated, immobilized and/or identified via such modifications.

Put another way, given that He et al. taught that such modifications can be included in proteins being translated in cell-free protein synthesis systems for the purpose of rapidly isolating, immobilizing and identifying the synthesized proteins, it would have been obvious to apply this known technique in order to improve the cell-free protein synthesis system of Kuroita et al. in the same way and achieve the expected results.

With respect to claims 6-11, Kuroita et al. teach kits comprising the reagent composition [0089]-[0091]. As discussed above, Zuk et al. also teach the advantages of providing reagents together in kit form. Therefore, it would have been further obvious to include the protein chip

reagent of Kuroita et al., He et al., and Zuk et al. as part of a kit for the art-recognized benefits of convenience and commercial sale.

***Response to Arguments***

25. Applicant's arguments filed 10/1/08 have been fully considered.

26. With respect to the rejections under § 103(a) as being unpatentable over Kuroita et al. in view of He et al. and Zuk et al., Applicant's arguments (Reply, pages 13-15) have been fully considered but are not persuasive.

Applicant argues that the composition of Kuroita et al. does not include mRNA; that He et al. does not describe freeze-dried preparations; and that Zuk et al. relates to reagents for immunoassays and not to cell-free protein synthesis compositions.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

In the instant case, while Kuroita et al. do not specifically teach including mRNA in the freeze-dried preparations, the teachings of Kuroita et al. and He et al. establish that a template was known to be a necessary ingredient for performing protein synthesis assays. When taken together with the teachings of Zuk et al. that it is a matter of substantial convenience to combine together as many reagents as possible together in kit form when performing assays, it is maintained that it would have been obvious to include template in the reagent of Kuroita et al.

***Conclusion***

27. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christine Foster whose telephone number is (571) 272-8786. The examiner can normally be reached on M-F 6:30-3:00. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark Shibuya, can be reached at (571) 272-0806. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Christine Foster/
Examiner, Art Unit 1641

/Christopher L. Chin/
Primary Examiner, Art Unit 1641